

FY15 Priorities

Project Title: Unsolicited Investigator Initiated Renewals

Mechanism(s): R01, R21, R34, R03, R13, D43, P30, P50, R24, U01, U10, P01, UM1

Competing Renewal, New or Expansion: 100% Competing Renewal

of Minority/International: 35%, I 12%

Plan Objectives(s): 1A, 1B, 1C, 2A, 2B, 2C, 2D, 2E, 2G, 5A, 5B, 5C, 5D, 6A, 6B, 6C, 6D, 6F, 6G, 6J, 7A, 7B, 8A, 8B, 8C

Narrative Justification:

NIDA supports a broad range of research on the substance use aspects of HIV/AIDS in diverse, substance using populations to reduce the acquisition and transmission of HIV associated with sharing injection paraphernalia and/or high risk sexual behavior, to improve HIV treatment including access and utilization of services, and to reduce the consequences of HIV/AIDS. To improve individual health and reduce HIV transmission to the community, NIDA supports studies of STTR, the seek, test, treat, and retain paradigm, which seeks out hard-to-reach substance using populations, tests them for HIV, links them to treatment and retains them in care. Research on substance abuse treatment as a component of HIV prevention as well as studies to enhance adherence and retention in combined substance abuse and AIDS treatment are also a significant component of NIDA's HIV/AIDS research. NIDA also supports research on the natural history, epidemiology, etiology and pathogenesis, prevention, and treatment of HIV/AIDS and AIDS-related co-infections (e.g., hepatitis B virus (HBV), hepatitis C virus (HCV), other sexually transmitted infections (STIs), and tuberculosis (TB)) and other comorbid conditions. Another research area supported by NIDA is basic research, including the use of animal models and in vitro systems to study the role of drugs of abuse in HIV/AIDS etiology and pathogenesis; neuroAIDS, genetics (host and viral genetic factors), epigenetics, proteomics, and systems biology are major areas of this program. Because HIV/AIDS associated with substance abuse knows no national boundaries, NIDA supports international research to reduce the intertwined epidemics of HIV/AIDS and substance use. NIDA also participates in collaborative efforts with other Institutes and Agencies in order to leverage resources and conduct complementary research in areas such as HIV and aging, and HIV and the CNS. NIDA has increased its research focus on alcohol abuse as a factor in HIV disease.

F 2015 Plan. This initiative is consistent with all the scientific objectives and emphasis areas in the NIH/OAR FY 201 Trans-NIH Plan for HIV-Related Research with the exception of Emphasis Areas #3 and 4, Microbicides and Vaccines. NIDA has FOAs that address a broad range HIV/AIDS issues including health disparities in the US, HIV prevention, and HIV/AIDS treatment for substance users. NIDA also contributes to collaborative efforts of CFARs, PHACS, ATN, HPTN, MACS, and WIHS. Through NIDA CTN, NIDA is supporting a study on retention in HIV care for HIV infected patients recruited from a hospital setting and a study on incorporating pharmacotherapy for opioid and alcohol addiction into HIV

treatment settings. The CTN is also conducting study in China aimed at improving receipt of HIV test results and enrollment in ART.

Project Title: Promoting Retention in HIV Care

Mechanism(s): R01, R21, R03, R34

Competing Renewal, New or Expansion: Expansion

of Minority/International: 60%, 10%

Plan Objectives(s): 5B, 5C, 5D

Narrative Justification:

The cascade of HIV care proposed by Gardner et al. has had a major impact on understanding the HIV epidemic in the U.S. Gardner et al. (CID 52, 793-800, 2011) calculated that only 19% of the HIV infected population in the U.S. had undetectable viral loads. CDC (MMWR 60/47 Dec. 2, 2011) did a subsequent calculation based on their surveillance data and estimated that 28% of HIV infected individuals in the U.S. have undetectable viral loads. In order for Treatment as Prevention to be effective in eliminating AIDS in a generation, the U.S. will have to greatly improve this number. Increased attention has been focused on HIV testing in order to reduce the number of HIV+ unaware of their infection. This is beneficial because it has been estimated that up to half of new infections are due to transmission from those who are unaware that they are HIV+. Generally, those who know that they are HIV+ reduce their risk behavior. In addition, identification of new infections enables individuals to engage in HIV care. But in many ways, increasing testing is low hanging fruit. Technologies enable individuals to learn their HIV status within minutes and testing can be performed in a variety of settings. After HIV diagnosis, the next stage in the cascade is linkage to care. Linkage to care is critical, and there are studies underway on linkage to care, including several funded under two Seek, Test, Treat, and Retain (STTR) RFAs. Data from ongoing NIDA funded studies on stages of the cascade will be able to be analyzed across studies because of resources devoted to harmonizing STTR data. However, long term retention in care has been less well explored. Recently published studies have highlighted how relatively few HIV+ are retained in care (Fleishman et al. JAIDS 60, 249-59, 2012; Hall et al. JAIDS 60, 77-82, 2012). In both studies blacks, younger patients, IDU had worse retention. Fleishman et al. using data from the multi-site HIV Research Network from 2001 to 2009 found that only 21% of all patients established HIV care, met retention criteria in every year, and were not lost to follow-up. Hall et al. analyzed CDC data from people living with HIV (PLWH) in 13 areas in the U.S. in 2009. Less than half of PLWH had laboratory evidence of ongoing clinical care and only two thirds established care within one year after diagnosis. Until there is a cure for HIV, PLWH will have to be retained in care throughout their life. A number of strategies have been employed to increase linkage and retention in care such as use of peer navigators, case management, incentives, use of technology such as cell phone reminders, but many issues remain in implementing these strategies individually and in combination. For example, while peer navigation has been adopted in many studies, there is no agreement on the elements that should be included in peer

navigation. In Africa, there are interventions involving the family and/or the community in maintaining PLWH in care, but there has been little research on adapting such strategies in the U.S. It is important to understand the patient and system level factors that contribute to poor retention. Retention in care is also a broader health care issue for all chronic diseases, and it is possible that strategies employed for other conditions can be adapted to HIV. Re-engagement in care of patients who have dropped out of care is a related issue which has also received little attention. Given that substance users may experience HIV treatment interruptions because of life events that they are more likely to encounter such as incarceration, loss of stable housing, it is important that studies be directed toward locating and re-engaging those who have dropped out of treatment.

Examples of studies under this initiative include;

- Research to identify the key elements of peer navigation
- Comparative effectiveness studies of different retention approaches
- International and U.S. studies that take advantage of local community resources
- Research exploring the use of incentives to enhance retention
- Innovative approaches to preventing loss to follow up

F 2015 Plan: This initiative is consistent with the NIH/OAR FY 2015 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science (Objectives: B, C, and D) targeting entry and retention and re-engagement in care.

Project Title: HIV Prevention in Vulnerable Populations in the U.S.—Emphasis on youth, the Homeless and Black/African American Women and Young Black/African American Men

Mechanism(s): R01, R21, R03, R34, U01

Competing Renewal, New or Expansion: Expansion

% of Minority/International: 85%

Plan Objectives(s): 1A, 1B, 1C, 5A, 5B, 5C, 5D

Narrative Justification:

As the US AIDS epidemic has evolved; ethnic/racial minorities, particularly African-Americans and Latinos bear an increasingly disproportionate share of new HIV infections and people living with HIV. While new infections have remained relatively stable, there has been an increased incidence of HIV among men who have sex with men (MSM), which is being driven by increases in young MSM who are members of ethnic/racial minority groups. NIDA has had a an ongoing program addressing vulnerable populations in the U.S., but it is now emphasizing research o homeless and unstably housed populations and Black/African American women (BAAW) and young Black/African-American men who have sex with men (YBAAMSM). This does not preclude studies o other vulnerable groups such Latinos/Latinas, Native Americans, MSM, etc.

Homelessness and marginal housing are associated with higher incidence of drug use, HIV and sexual risk behaviors, HIV infections, and poorer health outcomes. Homelessness and unstable housing are also associated with unemployment, recent incarceration, family dissolution, mental illness, and other health problems. Reducing HIV-related mortality and morbidity among the homeless requires comprehensive and integrated prevention and health care delivery systems that work effectively across multiple systems within the public and private sectors (child welfare, juvenile justice, criminal justice, education, and other social service systems). Given the current resource constraints on health delivery systems, new approaches are needed to ensure effective and efficient delivery and use of HIV/AIDS and substance abuse prevention and treatment services among homeless and unstably housed populations. Vulnerable homeless populations exist across the life span. Important gaps remain in serving youth, particularly ethnic minority gay youth, who have particularly high rates of homelessness and new HIV cases. Although urban Native Americans are overrepresented among homeless populations, and homelessness has been associated with substance abuse and HIV risk behavior, very little research has focused on this sub-population. Additional vulnerable homeless populations requiring greater attention include: youth in and transitioning out of the foster care system, run away youth, women, and military veterans.

There are a number of common features that appear to be important in the HIV risk of Black/African American women (BAAW) and young Black/African American men who have sex with men (YBAAMSM). These include social and structural factors such as fewer economic resources and less access to health care. Histories of trauma are more common, along with exposure to discrimination and experience of its pernicious consequences. In addition, the diversity of Black/African-American populations, which include immigrants and culturally distinct groups from Latin America, the Caribbean and Africa, has been under-appreciated, and elucidation of principles to enable implementation under a variety of cultural contexts is needed. Black/African Americans are in need of better interventions for HIV prevention, with consideration of cultural and structural factors, which may account for racial/ethnic disparities.

At the population level HIV treatment is HIV prevention, and it is essential that minorities be engaged in HIV testing, linkage to care, and retention in ARV therapy (seek, test, treat, and retain). At every step of the HIV cascade of care, minorities are less engaged than the general population. Although just as likely to have had HIV testing as other racial/ethnic groups, Blacks/African Americans tend to be diagnosed later than Caucasians. Sexual networking patterns and concurrent STI may be significant contributors to the dissemination of HIV among Black/African Americans, particularly within defined geographic areas. HIV risk may be greater in Black/African-American communities because of sexual mixing patterns that involve a greater proportion of same-race partners and more partnerships that cross socio-economic lines. Drug use and/or drug using sexual partners are important areas for study among diverse BAAW.

Black/African American men represented 11% of the male population in the U.S. in 2010, but 42% of HIV infection diagnoses. Black/African-American men who have sex with men account for disproportionate numbers of new cases, particularly among younger men. This is the one population segment where the numbers of new cases has continuously grown in recent years. Knowledge of HIV status is less common than among their Caucasian counterparts, and despite comparable rates of ever receiving HIV testing, the frequency of testing is lower and diagnosis of HIV is more likely to occur in the context of HIV-attributable symptoms. Incidence appears much greater among YBAAMSM under 25 and most of the HIV+ men in this age group are not aware of their HIV status. Moreover, the stigma and discrimination associated with drug use and HIV along with being MSM creates an environment which can serve as a deterrent from getting tested and seeking HIV treatment for YBAAMSM. HIV sexual and substance use risk behaviors among YBAAMSM tend to occur at similar levels when compared to their Caucasian counterparts, and in some studies less drug use and more condom use has been reported. On the other hand, patterns of substance use differ with more use of cocaine-based stimulants, different classes of "club drugs," and less use of methamphetamines than Caucasians. Higher rates of STIs among MSM, and among Black/African American communities generally combine with mixing patterns and keep STIs and HIV within the Black/African American community and pose network-based challenges to prevention. A growing number of prevention interventions targeting Black/African-American MSM with evidence of efficacy have become available in recent years, along with adaptations for Black/African-American cultural contexts of previously developed, efficacious interventions. Yet, these interventions generally do not address the developmental needs of YBAAMSM, and there has been no integration of what has been learned from effective substance use prevention among youth. Syndemic approaches to

characterizing risk have begun to be used with this population, but this knowledge and perspective has not been integrated into existing interventions. The impact of the Affordable Care Act on health care utilization and related risk and comorbid conditions in BAAW and YBAAMSM is another important area for study.

- Develop and test treatment models that integrate effective substance use treatment and HIV prevention and care interventions tailored to BAAW and/or YBAAMSM, and the health care settings they are most likely to use.
- Assess the role and impact of the Affordable Care Act on the integration into the health care system of prevention services for substance use, HIV, and comorbid conditions by BAAW and/or YBAAMSM.
- Develop and test prevention interventions that tailor elements of the Seek, Test, Treat and Retain model of HIV prevention to the social context of BAAW, YBAAMSM, and settings most used by these populations.
- Assess social and sexual network influences on substance use, sexual risk behavior, and HIV prevalence/incidence, with consideration of concordance among sexual and drug use networks, including potential effects of YBAMSM partnerships with women.
- Characterize developmental influences on substance use and sexual risk factors (including lifespan development) for HIV sexual and substance use risk among BAAW and/or YBAAMSM.
- Minorities are disproportionately represented in the criminal justice system and HIV is much more prevalent in the criminal justice system than the general population; therefore interventions tailored to this population, such as increasing HIV and HCV testing in jails and facilitating linkage to care and retention in care for prisoners post-release are encouraged.

F 2015 Plan: This initiative is consistent with the NIH/OAR FY 2015 Trans-NIH Plan for HIV-Related Research for Natural History and Epidemiology (Objective A) by characterizing risk factors in vulnerable populations, (Objective B) by evaluating factors influencing uptake and adherence to all steps of the testing and treatment process, and (Objective C) by ensuring that domestic epidemiological studies accurately represents populations at risk for HIV/AIDS. This initiative also supports Behavioral and Social Science (Objectives: A, B, C, and D) in developing, evaluating, and advancing prevention interventions (at both the individual and community level); conducting basic and behavioral research on factors influencing HIV risk behaviors and on the consequences of HIV disease; conducting treatment, health, and social services research for people infected and affected by HIV; quantitative and qualitative research to enhance HIV prevention and care, and collaborative efforts with other ICs in networks such as MACS, PHACS, HPTN and ATN. By focusing on prevention in vulnerable populations in the US, this initiative seeks to reduce disparities in disease transmission and acquisition.

Project Title: Developing Comprehensive Interventions for Substance Using MSM

Mechanism(s): R01, R34

Competing Renewal, New or Expansion: Expansion

of Minority/International: 35%, I 10%

Plan Objectives(s): 1A, 1B, 1C, 5A, 5B, 5C, 5D

Narrative Justification:

MSM continue to be disproportionately affected by HIV. CDC's current estimates indicate that HIV diagnoses among MSM are 44-86 times greater than for other men, and 40-77 times that of women in the US. In addition to ongoing transmission among MSM in the US, MSM have emerged as a population at considerable risk for HIV in parts of Asia, epidemics have re-emerged in parts of Europe, and HIV among MSM communities in Africa is beginning to be identified. Hepatitis C (HCV) monoinfection and coinfection with HIV are increasingly prevalent among MSM. It is particularly important that HIV infected MSM be screened regularly for HCV because HIV positive MSM are at higher risk of acquiring HCV than HIV negative MSM. While injection drug use is a risk factor for HCV, in MSM noninjection drug use is frequently associated with sexually transmitted HCV. Substance abuse is common among MSM in the US and, increasingly in international regions such as Asia, and is associated with elevated risk of acquisition or transmission of HIV and HCV through risky sexual behaviors. Methamphetamine use, in particular, has been identified as a driver of risk among MSM, in part because of its motivational effects on behavior. Other stimulant use is common, particularly cocaine and crack, as well as the use of "club drugs" (e.g., ecstasy), and alcohol; poly-substance use is common. Drug treatment intervention research typically has not targeted MSM and efficacious pharmacological interventions are not yet available for stimulants. Behavioral interventions have shown mixed effects; reductions in sexual risk behavior may not be sustained. There is a continuing need for new and novel interventions, including more effective pharmacological and behavioral treatments for stimulant use and specialized interventions (pre-exposure prophylaxis, post-exposure prophylaxis) that address high risk sexual behavior associated with episodic, poly-substance use. Substance use, particularly stimulant abuse, has been a barrier to adherence to HIV medications. Studies are needed in MSM to determine whether substance use interferes with the effective use of medication-based pre-exposure prophylaxis (PrEP) or post-exposure prophylaxis (PEP). High risk MSM who also engage in injection risk behavior may be important targets for PrEP because PrEP has also been shown to be efficacious in preventing injection related HIV transmission. This priority supports the development of comprehensive, multidisciplinary approaches that focus on the interdependent nature of sexual and substance use risk, as well as effects of substance use on adherence to antiretroviral treatment (ART) for HIV treatment and for prevention (including PrEP). This would include behavioral and pharmacological approaches to treating stimulant dependence and integrated service delivery systems for managing drug treatment and ART.

This priority includes, but is not restricted to:

- Development and evaluation of novel behavioral and pharmacological treatments for stimulants among MSM.
- Implementation and evaluation of interventions that integrate HIV transmission prevention, substance abuse treatment, and treatment for HIV and the complications associated with HIV therapeutics into single systems of care, with attention to long-term management of co-morbidities (e.g., HCV, HBV, STIs), medical consequences and disease progression.
- Interventions to encourage sexually active and/or substance-using HIV-infected MSM to receive routine and repeated HCV screening to allow for early diagnosis and treatment of HCV.
- Evaluation of substance use effects on PrEP, PEP, and ART uptake and adherence
- Evaluation of longitudinal patterns of drug use among MSM, with attention to how use changes between and among substances and how substance use is associated with sexual risk behaviors that facilitate HIV acquisition and transmission.
- Retrospective studies with rigorous non-experimental designs (e.g., case-control) that evaluate how substance use is managed over time by MSM, with attention to factors related to avoidance or reduction of substance to develop resilience-based interventions.
- Studies of interaction between aging and HIV in MSM.

FY15 Plan: This initiative addresses disparities based on sexual identity and addresses MSM, the group in the US that bears the highest burden of HIV/AIDS and is focus of the National strategy. MSM are also an important risk group internationally, where substance use is also factor in high risk behavior. The research supports emphasis areas Natural History and Epidemiology as well as Behavioral and Social Sciences.

Project Title: Implementation Science Research

Mechanism(s): R01, P01, U10, UM1

Competing Renewal, New or Expansion: Expansion

of Minority/International: 35%, I 25%

Plan Objectives(s): 1A, 1B, 1C, 5A, 5B, 5C, 5D

Narrative Justification:

Efficacious interventions developed to prevent or treat HIV/AIDS in a particular setting often yield disappointing results on scale-up in diverse settings. Another issue is how to choose between competing interventions. Implementation science research is the multidisciplinary field that addresses such issues. Implementation science research seeks to understand the etiology of gaps between expected results and observed outcomes. Implementation science studies the effectiveness and cost-effectiveness of interventions; its goal is the integration of research findings and evidence-based interventions into healthcare policy and practice and, hence, to improve the quality and effectiveness of prevention, treatment, health services and care. Implementation science research recognizes that the environment, economics, culture, gender, behavior, and social circumstances are all factors that may complicate adapting interventions from one setting or population to another. Because drug abuse is stigmatized and often dealt with punitively rather than from a public health perspective, implementation science research may be particularly useful in identifying barriers and testing possible solutions for HIV/AIDS interventions in drug using populations. The ultimate goal of implementation research is to determine how best to provide a comprehensive, integrated mix of high quality, sustainable, cost-effective interventions to reduce HIV risk behavior and infections.

Implementation gaps in the U.S. and internationally that this initiative addresses include but are not limited to:

Combination, integrated prevention--While advances in HIV prevention and treatment make it now possible to look forward to a generation without AIDS, understanding how to evaluate local epidemiologic data and then develop programs to meet local needs for combination, integrated prevention is critical. There is no one size fits all; prevention must be tailored to local conditions and resources. Epidemiologic data are needed to guide prevention efforts, but reliance on national or state-wide data may not capture local conditions and/or may not be available in many resource poor settings. Focusing on gathering local data from high risk groups may provide sentinel data to focus prevention efforts. In addition, it is important to assess the local social, economic, and policy environments in which risk behavior occurs and which will affect the choice of interventions. Evaluation of resources available for HIV prevention and modeling different scenarios can help to determine the most cost-effective approach for a given setting. The constituents of comprehensive prevention and the integration of these components will also vary. Combination prevention has been defined by UNAIDS as, "The strategic, simultaneous use of different classes of prevention activities (biomedical, behavioral, social/structural)

that operate on multiple levels (individual, relationship, community, societal), to respond to the specific needs of particular audiences and modes of HIV transmission, and to make efficient use of resources through prioritizing, partnership, and engagement of affected communities.” To further enhance this prevention approach, this initiative calls for integrating as well as combining interventions. Integration would be more than co-localization of services—it would aim to use the same team to deliver a variety of interventions. For example, ART and drug abuse treatment and treatment for co-infections and risk reduction counseling could be provided by the same staff that provides linkages to housing and other assistance.

To date, several promising integrated behavioral and biomedical treatments and approaches have shown positive outcomes in decreasing the rate of new HIV infections, promoting greater adherence to HIV treatment and overall medical management, improving engagement and retention in HIV care, and reducing substance abuse. However, there remains a large gap regarding translation from research models into combination approaches that are effective in “real world” settings, such as front-line community based organizations, substance abuse treatment venues and other direct providers of clinical care. Maximizing adherence in the broadest sense is key to effective implementation. Specifically, this initiative seeks to explore mechanisms to successfully transfer and sustain efficacious integrated combination preventive and treatment interventions (e.g., targeting use of and adherence to ART, screening and risk reduction, engagement and long-term maintenance in HIV care, and overall medical management for co-morbid conditions, such as substance use, mental health impairments, Hepatitis C, TB) for at-risk and HIV+ populations in real-world practice settings. This may include investigating the optimal settings and approaches for intervention delivery (primary care, urgent care and/or specialized care settings, home) as well as structured analysis of local community resources to understand the capacity needed to deliver the optimal “dose” of required treatment. In short, it is critical to understand how evidence-based interventions are transported into and maintain their potency in real-world community-based practice settings (e.g., ERs, primary care, criminal justice settings, drug treatment etc.).

New methodologies are needed to evaluate the effectiveness of combination prevention. Randomized controlled trials using incidence as an endpoint have to be very large and limited to settings with high incidence. Even with limited HIV prevention efforts to date, these settings are becoming rare. Therefore, alternative study and evaluation designs are needed.

ART as HIV prevention- Engaging and retaining substance users in care: initiating care earlier in the course of HIV infection and long-term retention in care are crucial to maximizing prevention opportunities, preserving the efficacy of first-line ART, and improving individual and population health outcomes. Examples of research topics include: 1) Testing of models to optimize coverage of care services; 2) Comparing models of service provision and adherence support; 3) Delineating key issues that result in suboptimal clinical outcomes; 4) Identifying appropriate portals for HIV testing; and 5) Identifying social and structural barriers as well as individual-level behaviors to improve ART initiation and maintenance.

Medication-assisted treatment (MAT) as HIV prevention-MAT is unavailable or of limited availability in many settings. In the U.S., MAT is limited or unavailable in criminal justice settings. In the U.S. physician adoption of buprenorphine/naloxone MAT has been relatively slow due to regulatory, financial, and attitudinal barriers. Yet, because buprenorphine/naloxone can be prescribed by physicians and dispensed at community pharmacies as opposed to methadone, which usually requires daily visits to a specialized clinic, there are advantages in terms of patient acceptability. In addition, because a specialized dispensing clinic is not required, it may be easier to integrate buprenorphine/naloxone treatment with HIV care in infectious disease clinics or primary care. Internationally, there are many countries with large numbers of IDUs and high HIV prevalence that have little or no MAT.

Implementation science research is needed on how best to expand MAT for a given setting. The use of MAT as a stand-alone intervention compared with integration of MAT with ART and treatment for comorbid conditions is another major area for study by implementation scientists. It will be important to determine which programs are most effective in expanding MAT coverage and the relationship between MAT coverage and reductions in risk behavior. In addition, studies should evaluate whether MAT leads to increased adherence to ART and improved HIV treatment success.

Long-lasting opioid pharmacotherapy with depot naltrexone—Intramuscular injection of extended release naltrexone can be used as a once a month treatment. In countries that do not allow opioid agonists to be used to treat opioid addiction, this medication assisted therapy offers an alternative. Similarly, long acting treatment with opioid antagonists may be more readily adopted in criminal justice settings. This therapy may also be beneficial in situations where adherence is an issue, where there are few health care staff, or where patients have to travel long distances to reach caregivers. Implementation research studies are needed on long-lasting opioid antagonists. It will be important to determine whether patients remain in treatment and to what extent they reduce their HIV risk behavior and/or maintain their adherence to ART.

F 2015 Plan: This initiative is consistent with the FY15 Trans-NIH Plan for HIV-Related Research Natural History and Epidemiology (Objectives A, B, and C) by supporting studies on the uptake and adherence to frequent HIV testing and linkage to and retention in care, studies on the cost-effectiveness of preventive interventions, determinants of HIV acquisition among vulnerable populations, research on substance abuse treatment modalities as HIV prevention interventions, evaluating the impact of substance abuse treatment on the effectiveness and, and consequences of ART, and encouraging more HIV prevention research in at-risk marginalized and vulnerable populations. It supports Behavioral and Social Sciences (Objectives A, B, C, D) by supporting research substance use and sexual transmission, designing and testing interventions for vulnerable populations, studying risk and protective behaviors associated with HIV transmission and progression in specific social and cultural contexts, studying barriers to health care utilization, refining techniques for measuring social networks and for collection of reliable information on sexual and drug-use risk behaviors. This initiative supports research on the feasibility, effectiveness, and sustainability required for scale-up and implementation of interventions for communities at risk in the US and internationally, and includes collaborative efforts with networks such as ACTG and HPTN.

Project Title: Transformative Research

Mechanism(s): DP1, R01

Competing Renewal, New or Expansion: New and expansion

of Minority/International: M 10%, I 5%

Plan Objectives(s): 1A, 2A, 2B, 2C, 5A, 6A

Narrative Justification:

NIDA Director's Avant-Garde Award Program for HIV/AIDS Research: In FY08, NIDA introduced the Avant-Garde award to encourage cutting edge, high-risk, high payoff HIV/AIDS research that has the potential to open new avenues of research and/or have broad public health impact by leading to new breakthroughs in HIV/AIDS prevention and treatment interventions for substance users. It uses the DP1 mechanism; the same mechanism as the NIH Director's Pioneer award. This ongoing program selects 2-awardees each year. Several Avant-Garde awardees are conducting studies that are highly relevant to efforts towards cure by focusing on strategies that may lead to new therapies to control or eliminate HIV. Among the funded projects are: studies of HIV reservoirs and latency, systems biology of immune reconstitution, proteomics of virus-host interactions, HIV transmission between cells, development of a mouse model containing human genes that regulate replication, pathogenesis, and immunity, public health approaches to prevention that combine behavioral/social science data with phylogenetic information to intervene in network transmission, and new therapeutic approaches suited to treat infections in populations with limited access to health care. Treatment as prevention in injection drug users was one of the projects funded in 2008, and several significant papers have resulted from this award, and the work is continuing under an Advancing Exceptional Research on HIV/AIDS award. In 2013 NIDA developed the Advancing Exceptional Research on HIV/AIDS award that utilizes an R01 mechanism and complements the Avant-Garde DP1. It supports research by individual and multiple principal investigators and is an ideal mechanism to support continuation of the research begun under the DP1 award.

FY15 Plan: This initiative attracts extremely creative scientists who wish to pursue high-risk, high pay-off research that has the potential to transform treatment and/or prevention for drug users. It includes basic and therapeutic research focused on elimination of viral reservoirs leading toward a cure. This initiative supports emphasis areas Etiology and Pathogenesis 2A, 2B, 2C and Therapeutics 6A. It also supports potentially transformative Behavioral and Social Sciences interventions 5A and Natural History and Epidemiology 1A, including STTR.

Project Title: Prevention and Treatment of HCV in Those with and at Risk for HIV

Mechanism(s): RPGs

Competing Renewal, New or Expansion: Expansion

of Minority/International: 35%, I 10%

Plan Objectives(s): D

Narrative Justification:

In the U.S. deaths from hepatitis C (HCV) now exceed those due to HIV. Most people living with HCV are unaware of their infection. HCV infection is closely linked to injection drug use, but awareness of HCV infections associated with sexual transmission among MSM has increased. As with HIV, African Americans have a higher rate of chronic HCV infection than other groups. Recently, an alarming increase in HCV among young nonurban injection drug users has emerged. HCV progression is enhanced by HIV coinfection. In a cohort of injection drug users, those with HCV and HIV had liver fibrosis stages similar to those a decade older who were not HIV coinfecting. Over the past decade, there have been dramatic improvements in HIV treatment that have led to reductions in deaths. The HIV Treatment as Prevention (TasP) holds promise for an AIDS-free generation. Yet, there have been improvements in HCV therapy with more to come. It has been suggested that a seek, test, and treat strategy may ultimately lead to the eradication of HCV disease. To this end, this initiative proposes research to improve HCV testing through encouraging use of rapid HCV in point-of-care testing in clinics and among populations at increased risk such as criminal justice populations. Models of care that integrate HCV treatment with primary care, substance abuse treatment and other services must be explored. Currently, HCV infected injection drug users have largely been excluded from HCV care. As new therapeutic agents become available, it is important to test for interactions with HIV antiretroviral drugs and medications used to treat substance abuse. Another promising area that NIDA supports genetic studies that have identified genes associated with spontaneous clearance of the HCV virus. Such studies are a step toward the development of personalized medicine for HCV. Because of the critical role that drug abuse plays in HCV disease, NIDA is conducting research aimed at breaking down barriers to accessing HCV screening, treatment, and prevention services.

F 2015 Plan: This initiative is consistent emphasis area 6D Therapeutics, Prevent and Treat Coinfections, in the NIH/OAR FY 2015 Trans-NIH Plan for HIV-Related Research as it pertains to prevention and treatment of HIV and HCV coinfection in drug using populations.

Project Title: Enhancing Treatment as Prevention through Use of Incentives and Technology

Mechanism(s): R01, R21, R34

Competing Renewal, New or Expansion: Expansion

of Minority/International: 40%, I 5%

Plan Objectives(s): 5A, 5B, 5C, 5D, 6B, 6D

Narrative Justification:

Evidence for the efficacy of HIV Treatment as Prevention (TasP) in diverse populations is accumulating. TasP is critically dependent on identifying those who are infected, linking them to care, and ensuring adherence to treatment, and retention in treatment. At each stage of the process incentives and interventions using technology such Ecological Momentary Assessment (EMA), Medication Event Monitoring System, cell phone and/or Digital Assistant Device may be useful. Cell phone minutes may even be used as an incentive. Motivational incentives have long been used to promote abstinence from drugs and to promote adherence to medications to treat drug abuse. Incentives have also been used to engage and retain drug users in drug abuse treatment. This initiative encourages the use of motivational incentives as a component of the continuum of HIV prevention and treatment including testing, engagement in treatment, adherence to treatment regimens, and retention in HIV care. Technology may also be used to improve HIV prevention and care in drug using populations. Technological instrumentation has been used to assess/monitor behavior and adherence in “real time”, including adherence to HIV treatment regimens, and monitoring of antecedents to drug use and HIV-risk behaviors, but as technology improves, the range of applications will increase. This initiative encourages the innovative use of technology to improve HIV prevention and treatment. The use of technology may vary by setting. In resource poor countries, technology has been used creatively to provide variety of health services.

Incentives and use of technology may be useful and cost effective in improving ART adherence in substance abusers. There have been several small randomized interventions trials, but the feasibility and cost-effectiveness of scaling up such interventions should be evaluated. In addition, interventions must be sustainable over the long term. Tailoring and evaluating community-friendly interventions is critical, given the financial constraints faced by resource-limited community-based clinics and treatment centers. Strategies based on behavioral reinforcement and use of technology may also be of value in retaining drug users in AIDS treatment and encouraging them to access related services. Studies are needed to compare interventions and combinations of interventions targeted to specific populations and settings.

The topics to be addressed by this initiative include:

- Assess what factors, information, and incentives would be necessary to motivate high-risk drug-using populations to understand the benefits of early detection of blood-borne viruses (HCV and HIV) and to undergo voluntary counseling and testing.
- How feasible is it to develop, utilize, implement, and/or disseminate technologies among drug abusing populations with HIV?
- Which groups and approaches are the most likely candidates for efficacious use of these technologies? What subgroups of drug-abusing populations with HIV (e.g., prisoners leaving correctional facilities and transitioning back to communities) are most suitable?
- Assess whether drug abuse treatment enhances initiation, adherence, and retention in HIV treatment.
- Study how to effectively use incentives and other motivational factors to enhance HIV testing, entrance into HIV care, adherence to ART and other treatment medication regimens, and retention in HIV treatment and reduction in viral load. Evaluate the subject characteristics (e.g., type and frequency of drug use), characteristics of the incentives program (e.g., individual or group contingency management; size and frequency of incentives), and other factors that influence effectiveness.
- Evaluate cost effectiveness of interventions using incentives and/or technology across different populations.
- Evaluate cost effectiveness of the use of incentives over different schedules of reinforcement.

F 2015 Plan: This initiative is consistent with the NIH/OAR FY 2015 Trans-NIH Plan for HIV-Related Research for Behavioral and Social Science research (Objectives: A, B, C, and D). It will be investigate the use of technology to encourage drug users to adhere to treatment intervention regimens, including adherence to ART therapy and the use of incentives to encourage drug users to access HIV/HCV testing and counseling services, return for follow-up diagnostic results, and enter and adhere to prevention and treatment intervention regimens, including adherence to ART and HCV therapy. It is also consistent with Therapeutics (Objective B and D) by supporting studies to improve adherence to ART regimens and regimens to treat coinfections.

Project Title: Training, Infrastructure, and Capacity Building

Mechanism(s): R24, R25, F 31, F32, T32, D43

Competing Renewal, New or Expansion: Expansion

of Minority/International: 20%, I 7%

Plan Objectives(s): 7A, 7B

Narrative Justification:

INVEST Fellowship Program and Humphrey Fellowship Program: The INVEST program brings foreign postdoctoral fellows to the U.S. for one year of research training and also includes professional development activities and grant-writing guidance. NIDA has added additional slots to this program dedicated to training investigators with an interest in HIV/AIDS research. This expansion of the INVEST program complements other efforts by NIDA to increase international research on HIV/AIDS. The Humphrey program is a partnership with the U.S. Department of State to support a unique training program for midcareer drug abuse professionals; some of NIDA's Humphrey fellows have an interest in HIV/AIDS. In addition, NIDA participates in the national Humphrey Fellowship seminar and has organized sessions focusing on HIV/AIDS and invited participation of fellows from Emory Humphrey Program, which has an HIV/AIDS concentration. Through contacts with NIDA staff, further interactions between foreign HIV/AIDS researchers and U.S. investigators have been facilitated.

A-START: To facilitate the entry of newly independent and early career investigators into the area of AIDS research, NIDA has developed the AIDS-Science Track Award for Research Transition (A-START) mechanism. This program supports feasibility studies using the R03 mechanism and providing up to \$100,000 direct costs for two years to facilitate the entry of new investigators into drug abuse and HIV/AIDS research.

Research Training: This program supports research efforts through institutional training research grants (T32), pre-doctoral (F31), post-doctoral (F32) mechanisms, as well as through collaborations with FIC. The NIDA Research Education Program for Clinical Researchers and Clinicians (R25) also supports careers as clinical researchers, clinicians/service providers, or optimally, a combination of the two and includes HIV/AIDS as a topic of interest. NIDA's Diversity-promoting Institutions Drug Abuse Research Program (DIDARP) (R24) also strongly encourages HIV/AIDS studies. To increase the numbers of underrepresented minorities in research careers in drug abuse research, including HIV/AIDS, NIDA supports a program of diversity supplements at the pre-doctoral, post-doctoral, and investigator level to train minority investigators in HIV/AIDS research. The purpose of all of these programs is to help ensure that a diverse and highly trained workforce is available to assume leadership roles related to the Nation's biomedical and behavioral research agenda in the areas of substance abuse and HIV/AIDS.

F 2015 Plan: This initiative is consistent with the NIH/OAR FY 2015 Trans-NIH Plan for HIV-Related Research for Training, Infrastructure, and Capacity Building (Objectives A and B) by supporting predoctoral, postdoctoral, and advanced research training across a broad range of AIDS-related disciplines. It is also consistent with the goal of establishing and maintaining the appropriate infrastructure needed to conduct HIV research domestically and internationally.